BMT CTN PROTOCOL # 0601
Unrelated Donor Reduced Intensity Bone Marrow Transplant for Children
with Severe Sickle Cell Disease (SCURT)

SUMMARY OF CHANGES
Modifications from Version 10.0 to 11.0

Deletions are indicated in strike-out text; additions are noted in underlined text.

§2.6.4 ~~Hypertension~~ Blood Pressure Monitoring and Control

~~Hypertension~~ Blood pressure should be ~~strictly~~ **strictly** controlled to prevent CNS toxicity. Blood pressure should be monitored closely (every four hours) and elevations in ~~both~~ systolic and/or diastolic pressure(s) should be treated ~~promptly~~ **promptly** to maintain blood pressure ~~at the patient's pre-transplant baseline ± 20%~~ within 10% above ~~of~~ the baseline age-related median systolic and diastolic pressure as described in children with SCD in *Pegelow et al Am J Med 1997; 102: 171-77*. Table I provides age-related medians of blood pressure in patients with sickle cell disease as published in the manuscript. In addition, close attention should be paid to fluid balance since fluid overload (patient weight is >10% of base weight in euvolemic state at the time of admission to the BMT unit) may contribute to elevations in blood pressures.

TABLE I

Medians and 90th Percentiles of Systolic and Diastolic Blood Pressure for Sickle Cell Anemia Subjects in the Cooperative Study of Sickle Cell Disease (CSSCD)

Age (Years)		2–3	4–5	6–7	8–9	10–11	12–13	14–15	16–17	18–24	25–34	35–44
Females N		257	97	72	68	57	71	89	81	227	199	66
SYS	Median	90	95	96	96	104	106	110	110	110	110	110
BP	90th	100	110	110	110	110	118	120	122	122	125	130
DIA	Median	52	60	60	60	60	62	70	70	64	68	70
BP	90th	62	70	70	70	74	74	80	78	80	80	84
Males N		276	111	78	66	75	61	75	53	179	166	41
SYS	Median	90	95	100	100	100	110	108	112	112	114	110
BP	90th	104	110	108	116	112	120	120	128	130	130	132
DIA	Median	54	60	60	60	60	64	64	70	68	70	70
BP	90th	66	68	68	70	70	72	78	80	80	80	84

SYS BP = systolic blood pressure; DIA BP = diastolic blood pressure.

§2.6.11 Supportive Care Guidelines for CNS Toxicities

Patients with sickle cell disease and cerebral vasculopathy have a high incidence of new CNS toxicities (seizures, labile hypertension, RPLS, PRES, intracranial hemorrhage, stroke, etc.) during the entire transplant process, beginning with the conditioning regimen and lasting through the time that immunosuppression is eventually discontinued. In order to minimize or avoid these risks, adherence to the following guidelines ~~is strongly recommended~~ **is necessary** for all BMT CTN #0601 patients:

1. The baseline blood pressure in patients with sickle cell disease is often less than "normal" for age. ~~Hypertension~~ Elevations in blood pressure can ensue following fluid infusions, or with the use of medications such as corticosteroids and calcineurin inhibitors, even after short term use. Blood pressure (both systolic and diastolic) **should** be monitored closely (at least every 4 hours) and ~~strictly~~ **strictly** maintained within ~~20% of the baseline blood pressure of the patient –~~ 10% above the median baseline blood pressure documented for that age in *Pegelow et al Am J Med 1997; 102: 171-77* (see section 2.6.4 for table). Aggressive (and often parenteral) use of anti-hypertensive drugs ~~may~~ **will** be required to control ~~hypertension~~ elevations in blood pressure. In addition, close attention should be paid to fluid balance since fluid overload (patient weight is >10% of base weight in euvolemic state at the time of admission to the BMT unit) may contribute to elevations in blood pressure.

Changes to Appendix B, Informed Consent to Participate in Research:
The following section was added to page B-11 after §*Potential Side Effects of Study Drugs* and prior to *§Risks and Toxicities Related to Standard Transplant Procedures*:

§Potential Risk of RPLS/PRES
The Data Safety and Monitoring Board (DSMB) of the Blood and Marrow Transplant Clinical Trials Network is a group of transplant, sickle cell disease and other experts that ensure the safety of patients treated on this and other trials. This group carefully monitors the experience of patients to make sure that the side effects that they experience are not unusual or more frequent or more severe than would be expected.

The DSMB has noted that children transplanted on the clinical trial BMT CTN 0601 have a higher than expected occurrence of a usually uncommon (<5%) complication called reversible posterior leukoencephalopathy syndrome (RPLS) also known as posterior reversible encephalopathy syndrome (PRES). Patients with RPLS/PRES have confusion and other changes in their ability to think. Sometimes, they experience seizures, sleepiness or, rarely, loss of consciousness. RPLS is diagnosed with an MRI of the brain. It is a disorder that is sometimes seen in patients with sickle cell disease even if they do not have a transplant. In transplant patients, it is usually caused by some of the drugs used to prevent or treat graft versus host disease. It can often, but not always, be prevented by very careful control of blood pressure. It is treated by changing graft versus host disease drugs, controlling blood pressure and/or giving anti-seizure medicines. About a quarter of the patients on BMT CTN 0601 have developed RPLS/PRES; all were successfully treated for this complication. Thus far, no RPLS/PRES has been observed in any patient more than 6 months from their date of transplant. We believe that children who are on prednisone or other corticosteroids, or immunosuppressive drugs such as cyclosporine or tacrolimus or have high blood pressure are more likely to develop RPLS/PRES.

If your child experiences any of these side effects or changes in mental status, you should contact your child's transplant physician right away, since early treatment is important. It is also important that any blood pressure medication be taken as prescribed to decrease the risk of RPLS/PRES.